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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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09/802,232 03/08/2001 Yoshihiko Makino JG-YY-5052 / 6671
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EXAMINER

LU, FRANK WEI MIN

ART UNIT

PAPER NUMBER

1655

DATE MAILED: 11/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/802,232

Applicant(s)

MAKINO ET AL.

Examiner

Frank W Lu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Location of Application

1. The Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1655.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in March 8, 2000 on Japan. It is noted, however, that applicant has not filed a certified copy of this foreign application as required by 35 U.S.C. 119(b).

Drawings

3. The original drawings submitted by March 8, 2001 have been approved by the office.

Specification

4. The disclosure is objected to because of the following informalities: a correct reference in lines 1 and 2 of page 13 should be Takenaka *et al.*, Chem. Commun., 10, 111 and 1112, 1998.

Appropriate correction is required.

5. The abstract of the disclosure is objected to because the abstract is not single paragraph. Correction is required. See MPEP § 608.01(b).

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Claim Rejections - 35 USC § 102/103

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 2, 5-12, and 15-20 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Piunno *et al.*, (Anal. Chem., 67, 2635-2643, August 1995).

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Piunno *et al.*, teach a fiber-optical DNA sensor for fluorometric nucleic acid determination.

Regarding claims 1, 2, 9-12, 19, and 20, Piunno *et al.*, teach to detect the association and dissociation of immobilized dT20 with dA20, rA20 and noncomplement DNA (dR19). The hybridization (forming double stranded complexes) between dT20 immobilized on a optical fiber (an oligonucleotide probe molecule on a solid carrier recited in claims 1, 10, 11, and 20), and dA20, rA20 and noncomplement DNA (dR19) were monitored by the use of the fluorescent DNA stain ethidium bromide and the dissociation of these double stranded complexes were determined by their melting curve (variation of temperature recited in claims 2 and 12) and monitored using UV-visible spectrometer (see abstract in page 2635, page 2639, Figures 3, 5, and 6, and Table 1 in pages 2641 and 2642). Note that dA 20 could be considered as a sample nucleic acid while rA20 could be considered as a reference nucleic acid recited in claims 1 and 11.

Regarding claims 5, 6, 15, and 16, ethidium bromide could be considered as the labeled intercalator having an electroconductive and fluorescent properties since a nucleic acid -ethidium bromide complex had fluorescence and could transfer electrons.

Regarding claims 7, 8, 17, and 18, dT20 could be considered as the probe molecule that contained a chain of a base sequence comprising at least three predetermined base units in series while rA20 could be considered as the reference nucleic acid wherein its fragment contained a chain of a base sequence comprising at least three predetermined base units in series which were

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fully complementary to the chain of the probe molecule since both dT20 and rA20 had 20 bp nucleotide and their sequence had known.

Although Piunno *et al.*, do not directly show to compare the stability between the sample and reference double stranded nucleic acid complexes, they detected the dissociation of double stranded nucleic acids by measuring decrease of quantity of the labeled intercalator on the solid carrier recited in claim 1 (see left column in page 2639, 2642, and 2643). Therefore, in the absence of convincing evidence to the contrary, this limitation is considered to be inherent to the reference taught by Piunno *et al.*, since Piunno *et al.*, could know the stability between the sample and reference double stranded nucleic acid complexes during the process of measuring decrease of quantity of the labeled intercalator on the optical fiber.

Alternatively, if applicant argues that Piunno *et al.*, do not show to compare the stability between the sample and reference double stranded nucleic acid complexes recited in claims 1 and 11 and ethidium bromide is not an electroconductive label recited in claims 5 and 15, the examiner noted that Piunno *et al.*, measured the dissociation of these double stranded complexes using their melting curve (see above) wherein the fraction of single stranded nucleic acid on the optical fiber in different temperatures could indicate how stability a double stranded nucleic acid complex was (see Figure 3 in page 2641) and the electroconductive intercalators for the electrochemical analysis of nucleic acid have been known in the art (see page 12 of the specification and for an example, see Takenaka *et al.*, Chem. Commun., 10, 111 and 1112, 1998). Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have

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detected the dissociation of double stranded nucleic acids and compared the stability between the sample and reference double stranded nucleic acid complexes by measuring decrease of quantity of the labeled electroconductive intercalator on the solid carrier. One having ordinary skill in the art would have motivated to modify the methods of Piuino *et al.*, because the detection of the dissociation of a double stranded nucleic acid using its melt curve has been known in the art at the time the invention was made and the simple replacement of a known method (using a melting curve) from another known method (measuring decrease of quantity of the labeled intercalator) for monitoring the dissociation and stability of a double stranded nucleic acid, and the simple replacement of one labeled intercalator with known properties (i.e., ethidium bromide) from another labeled intercalator with known properties (i.e., an electroconductive intercalator) would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

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9. Claims 4 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piunno *et al.*, (1995) as applied to claims 1, 2, 5-12, and 15-20 above.

The teachings of Piunno *et al.*, have been summarized previously, *supra*. Although Piunno *et al.*, did not directly disclose to dissociate double stranded nucleic acids in the presence of varied ionic strengths, Piunno *et al.*, did suggest that the duplex stability in low ionic strength buffers was less than that in high ionic strength buffers (see left column in page 2641).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have detected the dissociation of double stranded nucleic acids and compared the stability between the sample and reference double stranded nucleic acid complexes in the presence of varied ionic strengths. One having ordinary skill in the art would have motivated to modify the methods of Piunno *et al.*, because it has been known in the art at the time the invention was made that the duplex stability in low ionic strength buffers is less than that in high ionic strength buffers, and the simple replacement of a known method (using varied temperature) from another known method (using varied ionic strength) for monitoring the dissociation and stability of a double stranded nucleic acid would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

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Also note that there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

10. Claim 3 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piunno *et al.*, (1995) as applied to claims 1, 2, 4-12, and 14-20 above, and further in view of Sosnowski *et al.*, (US Patent No. 6,051,380, filed on December 5, 1997).

The teachings of Piunno *et al.*, have been summarized previously, *supra*.

Piunno *et al.*, did not disclose to dissociate double stranded nucleic acids using varied electrophoretic potential.

Sosnowski *et al.*, do teach to electronically denature double stranded nucleic acids. Note that polarity at microlocation in a self-assembling microelectronic device was reversed and voltage was applied to separate the two strands (see columns 60 and 61).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have detected the dissociation of double stranded nucleic acids and compared the stability between the sample and reference double stranded nucleic acid complexes using varied electrophoretic potential. One having ordinary skill in the art would have motivated to modify the methods of Piunno *et al.*, because it has been known in the art at the time the invention was made that double stranded nucleic acids could be electronically separation by denaturation and the simple replacement of a known method (using varied temperature) from another known method (using varied

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electrophoretic potential) for monitoring the dissociation and stability of a double stranded nucleic acid would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

11. No claim is allowed.
12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

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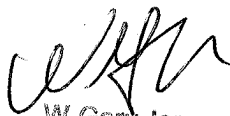
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
November 13, 2001


W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600